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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/087,466	03/01/2002	Alexander Olek	81659A	6657

23685 7590 11/17/2008
KRIEGSMAN & KRIEGSMAN
30 TURNPIKE ROAD, SUITE 9
SOUTHBOROUGH, MA 01772

EXAMINER	
BRUSCA, JOHN S	

ART UNIT	PAPER NUMBER
1631	

MAIL DATE	DELIVERY MODE
11/17/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/087,466	OLEK ET AL.	
	Examiner	Art Unit	
	John S. Brusca	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,14-18,20-23,25,26,30-34,36 and 41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12, 14-18, 20-23, 25, 26, 30-34, 36, and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-12, 14-18, 20-23, 25, 26, 30-34, 36, and 41 are pending.

Claims 1-12, 14-18, 20-23, 25, 26, 30-34, 36, and 41 are rejected.

Claim Rejections - 35 USC § 101

2. The rejection of claims 1-12, 14-18, 20-23, 25, 26, 30-34, 36, and 41 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter in the Office action mailed 14 January 2008 is withdrawn in view of the amendment filed 17 July 2008.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-12, 14-18, 20-23, 25, 26, 30-34, 36, and 41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a diagnostic or therapeutic method comprising determining genes that have differences in expression and methylation by comparison of two cancerous

biological samples. The specification describes a method of determining genes that have differences in expression and methylation relative to two groups of samples on page 11, relative to healthy and/or diseases samples on page 12, and relative to prostate cancer cell lines and healthy prostate cells on page 21. The specification does not describe a diagnostic or therapeutic method of determining genes that have differences in expression and methylation by comparison of two cancerous biological samples.

5. Applicant's arguments filed 17 July 2008 have been fully considered but they are not persuasive. The applicants point to the paragraph bridging pages 21-22 for support of a diagnostic or therapeutic method of determining genes that have differences in expression and methylation by comparison of two cancerous biological samples. The cited passage states "at least one biological sample is derived from biological material of healthy and/or diseased individuals." This recitation does not describe a comparison of two samples, both of which are cancerous. The applicants point to the term "and/or" as supporting the claimed subject matter, but the passage as a whole does not indicate that both samples are cancerous and the rejection is maintained.

6. Claims 1-12, 14-18, 20-23, 25, 26, 30-34, 36, and 41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In In re Wands (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation." These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must use a diagnostic or therapeutic method of determining genes that have differences in expression and methylation by comparison of two cancerous biological samples. For the reasons discussed below there would be an unpredictable amount of experimentation required to make the claimed invention.

b) The specification presents guidance on pages 14-18 to compare healthy and diseased samples.

c) The specification presents a working example on page 21 of comparison of prostate cancer cell line cells to healthy prostate cells.

d) The nature of the invention, molecular diagnostic assays, is complex.

e) Huang et al. shows a method of determining methylation sites relevant to breast cancer. Huang et al. shows in the abstract and throughout that the comparison was done between breast cancer cells and **normal** tissue so that differences that correlate with breast cancer could be determined.

f) The skill of those in the art of molecular diagnostic assays is high.

g) It is predictable from prior art such as Huang et la. that qualities of cancerous samples that are relevant to disease for diagnostic or therapeutic purposes should be compared to normal tissue controls so that the changes are known to appear only in diseases tissue.

h) The claims are broad in that they require determinations of gene panels useful for diagnostic or therapeutic purposes to be determined without determining whether the gene panels contain genes whose expression and methylation levels correlate with disease.

The skilled practitioner would first turn to the instant specification for guidance and working examples to practice the claimed method of making gene panels. However, the specification does not provide such guidance or working examples. Next, the skilled practitioner would turn to the prior art for such guidance. The prior art shows that genes related to disease should be assessed relative to normal tissue controls. Finally, said practitioner would turn to trial and error experimentation to make and use the claimed subject matter, which represents undue experimentation.

7. Applicant's arguments filed 17 July 2008 have been fully considered but they are not persuasive. The applicants state that meaningful information could be obtained while practicing the claimed subject matter if a benign sample was compared to a cancerous sample. The ordinary meaning of the term benign is not cancerous, and such an embodiment is not within the scope of the claimed subject matter and the argument is not persuasive. Even if, arguendo, benign tissue were considered to be cancerous, the claimed subject matter does not require one of the

cancerous samples to be benign, and the scope of the claims includes embodiments in which both samples are cancerous. A review of the specification does not reveal the term benign as part of the written description at the time of filing, and it is not apparent that comparison of benign and cancerous tissues, however the applicants may intend that the samples differ, were described or enabled by the instant specification. The rejection is maintained.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 571 272-0714. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie A. Moran can be reached on 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/John S. Brusca/

Primary Examiner

Art Unit 1631

jsb